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Invited Commentary | Oncology

Exploring the Causes of Death Among Patients With Metastatic Prostate Cancer—A Changing Landscape

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Using data from the Surveillance, Epidemiology, and End Results program, Elmehrath and colleagues[1] undertook a large retrospective cohort study of 26 168 patients with metastatic prostate cancer to determine the common causes of death in this population. Patients were followed up from the date of diagnosis to death or the end of the study period in 2016, and standardized mortality ratios were calculated (SMRs) for each cause of death. Most deaths occurred within 2 years of diagnosis (9869 of 16 732 deaths [59.0%]). Black patients had a higher risk of excess death overall compared with White patients (SMR, 6.68 [95% CI, 6.45-6.91] vs 5.66 [95% CI, 5.57-5.76]). Of all deaths in the cohort, 13 011 (77.8%) were due to prostate cancer, with 924 (5.5%) due to other cancers and 2797 (16.7%) due to noncancer causes. Cardiovascular disease (SMR, 1.34; 95% CI, 1.26-1.42), cerebrovascular disease (SMR, 1.31; 95% CI, 1.13-1.50), and chronic obstructive pulmonary disease (SMR, 1.19; 95% CI, 1.03-1.36) were the most common noncancer causes of death, and noncancer deaths were more common among older patients and patients with longer latency periods from diagnosis to death.

Recognizing the limitations inherent to SMR estimates, this study[1] is important considering that most patients with prostate cancer survive their disease for several years after diagnosis. As such, identifying the causes of deaths among these patients may help with multidisciplinary treatment planning. Elmehrath et al[1] postulate that hormone therapy treatments may increase the risk of cardiovascular and cerebrovascular disease in patients treated for metastatic prostate cancer, a theory that is supported by some epidemiological and biomedical evidence. Their finding of increased suicide rates among Asian or Pacific Islander patients and White patients with metastatic prostate cancer is a surprise and should be investigated further, considering that such deaths are potentially preventable.

Prostate cancer incidence in the US and other Western countries has increased significantly in recent decades, largely as a result of the widespread use of prostate-specific antigen (PSA) testing.[2] However, the incidence rates in countries like the US are stabilizing[2] following national recommendations to reduce PSA testing.[3] Mortality from prostate cancer over the same period has decreased,[4] which is thought to be associated with a combination of PSA testing detecting some cases of prostate cancer earlier, resulting in a lower incidence of metastatic disease at diagnosis, and greater availability of more-effective treatments for advanced disease.[2] Systemic therapies for prostate cancer, such as hormone therapy and chemotherapy, are not without their adverse effects, including increased risk of cardiovascular disease and other cancers, as highlighted by Elmehrath and colleagues.[1] This is particularly relevant for prostate cancer, which has a high long-term survival rate compared with almost all other cancer types,[4] and signals the need for greater holistic care for patients receiving these treatments.

Prostate cancer is expected to remain the most common cancer diagnosed in male individuals in high-income countries in the next decade, with incidence in low-income and middle-income countries projected to increase much more rapidly in comparison.[5] As observed in this study,[1] most patients with metastatic prostate cancer die from it, rather than other possible causes of death, reinforcing the need for innovations to promote early-stage diagnosis. The recent development and implementation of new tests for prostate cancer detection may reduce the proportion of patients who receive a diagnosis at a late stage, although some metastatic disease at the time of diagnosis will likely still occur. Multiparametric magnetic resonance imaging (mpMRI) of the prostate before biopsy

is one such test and has been shown to increase the detection of clinically significant prostate cancer compared with transrectal ultrasound–guided biopsy. mpMRI can also be used to guide prostate biopsy to reduce the risk of missed diagnoses that occur with transrectal ultrasound–guided biopsy biopsy.[6] PSA testing is known to be falsely normal in some men with aggressive and/or metastatic disease,[2] so the wider use of mpMRI may detect more clinically significant cancers earlier and help to reduce the burden of advanced prostate cancer in the future.

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